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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,226	08/19/2003	Ashley I. Bush	0609.4810002	3164

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EXAMINER	
DUTT, ADITI	
ART UNIT	PAPER NUMBER
1649	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/28/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/643,226	BUSH ET AL.	
	Examiner	Art Unit	
	Aditi Dutt	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36 and 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *8/19/03&10/10/06* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Status of Claims

1. The amendment filed on 10 October 2006 has been entered in full. Claim 36 has been amended. Claims 4-17, 24-35 and 38 are canceled.

2. Claims 36 and 37, are pending in the instant application. Claims 36 and 37 are under examination in the instant office action.

3. The text of any section of 35 U.S.C. not reiterated in this office action can be found in a previous office action.

4. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicants response and withdrawn.

5. Applicant's arguments filed on 10 October 2006, have been fully considered. New grounds of objection and rejection are as follow.

Information Disclosure Statement

6. Applicant's submission of copies of References AR52 and AR67 have been acknowledged. However, Applicant is required to submit a new USPTO 1449 form having the two above references for consideration.

102 and 103 rejections

7. Applicant's submission of Declaration of Kevin J. Barnham, PhD., submitted under 37 C.F.R. § 1.132 is effective to overcome the rejections under 102(b) and 103(a) in the previous office action.

Claim Objections

8. Claim 36 format is objected under MPEP § 608.01(i) [R-3], which states, (i) Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation.

Appropriate correction is required.

New grounds of rejection

Claim Rejections - 35 USC § 112

9. Claims 36 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

10. Regarding claim 36, the phrase "capable of" renders the claim indefinite because it is unclear whether the limitations following the claim are part of the claimed invention. Clarification is required.

11. Claim 36 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap

between the steps. See MPEP § 2172.01. The omitted steps are: step of obtaining or preparing the Aβ sample.

12. Claim 37 is indefinite because it depends from an indefinite claim.

Claim Rejections - 35 USC § 112-Lack of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 36-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

14. Claims 36-37 are drawn to a method of identification of a candidate pharmaceutical agent to be used in the treatment of AD, by incubating an Aβ sample with a redox-reactive metal in the presence or absence of the candidate agent followed by the determination of Aβ cross-linking.

15. The specification of the instant application teaches that intracellular concentrations of metal ions, such as copper and zinc, are significantly higher than the extracellular concentrations in the brain. The specification further teaches that any injury or changes in energy metabolism can result in the release

of metal ions in the extracellular space, inducing membrane bound Aβ to form aggregates (page 21, lines 11-22). The specification discloses the presence of Aβ aggregates induced by copper and zinc in AD affected brains (page 22, lines 28-29, pages 41-42). Furthermore, the specification demonstrates copper induced aggregation of Aβ peptide in vitro, which is abolished by mannitol (page 42, lines 20-22; Figure 9). However, the specification of the instant application does not teach any methods or working examples that indicate the administering of the agent in vivo that would result in a successful treatment of AD. In vitro experiments are vastly different both physiologically and in effectiveness as well as predictability of success, more so if the utility is driven towards complex and chronic illnesses such as AD. It would require undue experimentation and making a substantial inventive contribution for one skilled in the art to practice Applicant's invention, as currently claimed.

16. Furthermore, in making a determination of whether the application complies with the enablement requirement of 35 U.S.C. 112 first paragraph, each claimed invention must be evaluated to determine whether there is sufficient guidance provided and supported by working examples to inform a skilled artisan how to use the claimed invention without undue experimentation. In the instant case, the specification provides no guidance on how to use the claimed method for the treatment of AD because there is no evidence or sound scientific reasoning presented in the case, that administration of a compound identified by the claimed method would be beneficial to treat symptoms of AD. Furthermore,

even though redox-reactive metal catalyzed Aβ cross-linking is implicated in aggregate and plaque formation in AD, there is no evidence that inhibition of cross-linking would successfully treat the disease, since there are multiple processes that contribute to the development of AD. Additionally, the most important part of the information received from patients with confirmed cases is not always consistent and compromises the hypothesis that increased levels of redox-reactive metal mediated cross-linking are being predictive of AD.

17. The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. In re Wands, 8 USPQ2d, 1400 (CAFC 1988).

18. Relevant art indicates that few clinical trials have been performed and the approach to treatment of AD shall remain somewhat empirical (Gilmore et al., Brit J Haematol 99: 245-256, 1997; page 250, para 1). For example, metal chelators for efficient AD treatment are still under investigation as these substances are required to cross the blood brain barrier (BBB) for effectiveness and be non-toxic. The route of administration of the candidate agent is also very important, as different routes will involve different absorption, distribution, metabolism and elimination rates (Todorich and Connor, Ann. N.Y. Acad. Sci. 1012: 171-178,

2004; page 176). The instant specification does not provide neither enough guidance for such method of treatment, nor working examples, which would show that the claimed method was successfully practiced, thus, requiring undue experimentation on part of one skilled in the art to discover how to practice the claimed invention.

19. In view of the lack of teachings and unpredictability of the art set forth earlier, and also the total absence of the working examples, the instant specification is not found to be enabling for a method of identification of a pharmaceutical agent for the treatment of AD. It would require undue experimentation and making a substantial inventive contribution for the skilled artisan to discover how to use Applicant's invention as currently claimed.

Conclusion

20. No claims are allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aditi Dutt whose telephone number is (571) 272-9037. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 5:00 p.m.

22. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

23. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov/. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AD
01 December 2006

OLGA N. CHERNYSHEV, PH.D.
PRIMARY EXAMINER